REMARKS

Reconsideration, entry of this response, and allowance of the above application are respectfully requested.

Claims 50-82 are pending in the subject application.

I. REJECTION UNDER THE DOCTRINE OF OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 50-82 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 6-53 of copending U.S. Patent Application 10/363,935.

Applicant respectfully requests that the rejection be held in abeyance pending the determination of allowable subject matter in this and the cited application. At that time, if the rejection is still an issue and the cited application has issued, Applicant will address the substance of the double patent rejection in an appropriate manner.

II. REJECTION UNDER 35 U.S.C. § 103

Claims 50-82 stand rejected as allegedly obvious under 35 U.S.C. § 103 over U.S. Patent No. 4,808,616 to Buzzetti et al. ("Buzzetti") in view of U.S. Patent No. 4,871,528 to Tognella et al. ("Tognella") and U.S. Patent No. 5,795,909 to Shashoua et al. ("Shashoua"). Applicants respectfully traverse the rejection under 35 U.S.C. §103(a) as obvious over Buzzetti in view of Tognella and Shashoua in view of the following remarks.

The Examiner contends that Buzzetti discloses exemestane as an agent that is useful in the treatment of hormone-dependent cancers in mammals. Buzzetti is also cited as showing that the effective amount of exemestane is about 10 to about 150-200 mg/day. The Examiner concedes that while "Buzzetti... does not expressly disclose the employment of exemestane in combination with the instant antineoplastic agent, epirubicin or docetaxel in pharmaceutical compositions and methods for treating breast cancer in humans and lowering the side effects in humans." (*Office Action* at 4.). Tognella is cited as a disclosure of mono- or polychemotherapy against tumors. The Examiner states that Tognella discloses that known anti-tumor agents, such as epirubicin, used in combination with other agents, is useful in the treatment of breast cancer to reduce the side effects caused by anti-tumor therapy. The Examiner also relies on Tognella as a disclosure of the synergistic effects observed using multiple agents in combination therapy. Finally, the Examiner relies on Shashoua as a disclosure of numerous antineoplastic agents, including but not limited to docetaxel and epirubicin, in combination with aromatase inhibitors, including but not limited to exemestane, are useful in the treatment of breast cancer to reduce side effects.

Establishment of *prima facie* obviousness requires three conditions. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that Tognella does not disclose, suggest, teach or motivate one of ordinary skill in the art to make the claimed invention, and there is no reasonable expectation that the claimed invention would produce synergistic results. Tognella only relates to the combination of GSH with cis-platinum, and further including cyclophosphamide, 5-fluorouracyl, doxorubicin, metaxanthrone, methotrexate, etoposide, vincristine, and bleomycin; none of which is an aromatase inhibitor.

Specifically, Applicants respectfully submit that Tognella's teachings are limited to combinations including GSH and do not provide the requisite motivation to arrive at the claimed invention. More specifically, Tognella teaches that the synergistic effect of GSH (Col. 4, lines 39-40) was "particularly surprising" because "GSH, administered alone, is completely devoid of any anti-tumoral activity" (Col. 4, lines 39-41). Further, all of the examples recited in Tognella relate to combinations including GSH.

Applicants submit that the alleged surprising and synergistic effects of GSH when used in combination with the other anti-cancer compositions, as recited in Tognella, would only motivate one skilled in the art to continue to research anti-cancer therapeutic combinations which only include GSH. Therefore, Tognella does not motivate one skilled in the art to make the currently claimed combination containing exemestane and epirubicin or docetaxel, which does not contain GSH.

Assuming *arguendo* that there is motivation to combine exemestane and epirubicin or docetaxel as claimed, Applicants respectfully submit that there is still no reasonable expectation that the claimed combination would provide synergistic effects. Relying on the Abstract in Tognella, the Examiner asserts that it is obvious to expect synergistic effects with the claimed invention (*Office Action* at 4). But the Abstract merely summarizes that the specific combinations in Tognella can be used in polychemotherapy to reach surprising results. Because Tognella only relates to the synergistic effects of GSH, Applicants submit that the Abstract should not be interpreted so broadly as to mean that every possible combination of cancer-fighting compounds is expected to produce synergistic effects. Given the entire field of oncology, with its vast and diverse array of drugs, each of which use a variety of different mechanisms, Applicants submit that Tognella cannot possibly be used to justify the notion that it is a reasonable expectation that every combination of compounds known anti-cancer compounds in the art would have synergistic results.

Applicants respectfully submit that the alleged synergistic results disclosed in Tognella would not lead one skilled in the art to expect synergistic results for combinations without GSH. Tognella provides no motivation or suggestion whatsoever that non-GSH containing combinations would produce synergistic effects. This is especially true in the instant case where the chemical and physiological nature of exemestane, epirubicin, and docetaxel are different

from GSH. Therefore, Applicants submit that Tognella cannot be interpreted so broadly to stand for the proposition that synergistic effects are expected (*i.e.* not unexpected) for every possible combination of anti-cancer compounds.

Accordingly, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness because the cited reference Tognella neither motivates one skilled in the art to make the claimed invention, nor is there a reasonable expectation that the claimed invention would produce synergistic effects.

Finally, Shashoua does not remedy the deficiencies of either Buzzetti or Tognella. Shashoua merely provides is a list of possible antineoplastic agents and the general instruction that the agents may be used alone or in combination. Shashoua does not specifically direct the skilled artisan to select docetaxel and/or epirubicin from among the many agents listed, and use these agents with exemestane, also one aromatase inhibitor of a list of a variety of aromatase inhibitors, nor does Shashoua provide the skilled artisan a reasonable expectation of successfully achieving a super additive effect, such as that disclosed in Tables 1 and 2 of the instant application.

Assuming *arguendo* that it would be *prima facie* obvious to combine the cited art as suggested by the Examiner, Applicant submits that the claimed combination has unexpected or surprising effects which could not have been predicted by a person of ordinary skill in the art.

Specifically, the combination of exemestane with epirubicin or docetaxel provided super-additive or synergistic antitumor effect, *e.g.*, the combination of exemestane and low dose epirubicin (75% CR+RP) or exemestane and high dose epirubicin (90% CR+PR) provided super-additive antitumor effect as compared with exemestane alone (44% CR+RP), low dose epirubicin alone (7% CR+RP) or high dose epirubicin alone (27% CR+PR) (*see* Table 1); and the combination of exemestane and docetaxel (92% CR+RP) provided super-additive antitumor effect as compared to exemestane alone (44% CR+RP), or docetaxel alone (41% CR+RP) (*see* Table 2).

Further, Applicants respectfully submit that the unexpected results in the subject application are commensurate in scope with the pending claims, as required under *Kerkhoven* (*see Kerkhoven* at 850). The data in Table 1 of the specification compare the effects of exemestane alone and in combination with epirubicin. Similarly, the data in Table 2 compare the effects of exemestane alone and in combination with docetaxel. Further, instant claim 1 relates to a composition comprising exemestane with either epirubicin or docetaxel. Hence, Applicants submit that it is clear that the breadth of independent claim 1 is commensurate in scope with the data. Therefore, Applicants submit that the evidence of unexpected or surprising results rebut a *prima facie* case of obviousness, as required under *Kerkhoven*.

Based on the above arguments, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

In view of the remarks, the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number provided.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

Respectfully submitted,

Date: May 23, 2006

Christian M. Smolizza
Attorney for Applicant
Reg. No. **46,319**

Pfizer Inc
Patent Dept., 150-5-49
235 East 42nd Street
New York, NY 10017-5755
(212) 733-**9094**